PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
REP07477WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/02618	17.06.2003	17.06.2002
International Patent Classification (IPC) or both national classification and IPC		
A61K31/395		
Applicant		
ARAKIS LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.01.2004	30.09.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/02618

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-3 as originally filed

Claims, Numbers

1-3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,3
	No:	Claims	2
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-3
Industrial applicability (IA)	Yes:	Claims	1-3
	No:	Claims	

2. Citations and explanations

see separate sheet

SECTION V

1. *References*:

   D1: WO 02 00195 A
   D2: WO 00 06121 A
   D3: Fasmer et al.: 'Antinociceptive effects of (+-)-, (+)- and (-)-nefopam in mice', J. Pharm. Pharmacol., 1987, 39; 508-511.

2. *Novelty* **(Art. 33(2) PCT)**

2.1 **D1** discloses compositions suitable for application to the mucous membrane of the nasal and buccal cavity. The analgesic may be *nefopam* (p. 12, l. 16).

D2 describes *nasal or inhalable medicinal aerosol formulations* (p. 22, l. 12) for delivery of active agents, for instance *nefopam* (p. 16, l. 22).

D3 reports on studies of the antinociceptive effects of (+-)-, (+)- and (-)-nefopam in mice.

2.2 In the animal studies reported on in **D3**, the different isomers of nefopam were administered *by injection*. A formulation for injection would as well be *suitable for nasal administration*; therefore, **novelty** can ***not be acknowledged*** for the subject-matter of claim 2.

2.3 However, the available prior art does not disclose a composition comprising the ingredients defined in claim 3 *nor* the use of ***(+)***-nefopam according to claim 1.

The subject-matter of claims 1 and 3 would thus appear to be ***novel***.

3. *Inventive Step* **(Art. 33(3) PCT)**

3.1 The *problem* to be solved in the present application is the provision of a medicament for the treatment of pain.

The *solution* of the present application resides in the provision of ***(+)-nefopam*** for the manufacture of a medicament for *intranasal* administration for the treatment of pain.

3.2 The closest cited prior art would appear to be **D2.**
D2 describes *nasal or inhalable medicinal aerosol formulations* (p. 22, l. 12) for delivery of active agents, for instance *nefopam* (p. 16, l. 22). Nefopam is listed in the group of *analgesics* (p. 16, l. 20-23); it is indicated that the active agents might be used in form of the *isomers, enantiomers or racemates* (p. 17, l. 28).

From the information given in **D2** it is clear that nefopam is known for the treatment of pain; intranasal administration of the compound is disclosed.

The *difference* between the prior art and the present claim 1 is therefore the limitation of claim 1 to ***(+)-nefopam.***

D3 discloses that the antinociceptive activity of *'(+)-nefopam* was significantly more potent than *(-)-nefopam'*.

Combining the information provided in **D2** and **D3**, it cannot be considered that a person skilled in the art would need any special inventive idea to conclude that ***(+)-nefopam*** would be useful for the manufacture of a medicament for intranasal administration for the treatment of pain.

3.3 As compositions comprising ***(+)-nefopam*** suitable for intranasal administration are already known (see *'novelty'*), and the nasal administration of nefopam (aerosol formulations) are as well known in the art, it would be a matter of routine for the skilled person to prepare *suitable formulations* (claim 3).

3.4 An ***inventive step*** could therefore ***not*** be ***acknowledged*** for the subject-matter of claims 1 and 3.

4. *Industrial Applicability* **(Art. 33(4) PCT)**

The requirements of industrial applicability would be fulfilled for the subject-matter of claims 1-3.